Complete Summary

GUIDELINE TITLE

Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the National Society of Genetic Counselors.

BIBLIOGRAPHIC SOURCE(S)

Bennett RL, Motulsky AG, Bittles A, Hudgins L, Uhrich S, Doyle DL, Silvey K, Scott CR, Cheng E, McGillivray B, Steiner RD, Olsen D. Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the National Society of Genetic Counselors. J Genet Counsel 2002 Apr;11(2):97-119. [74 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Genetic disorders, such as:

- Birth defects
- Metabolic disease (diseases of amino acids, organic acids, urea cycle, galactosemia, lactic acidosis, glycogen storage disease, lysosomal storage disease, peroxisomal and mitochondrial respiratory chain dysfunction)

GUIDELINE CATEGORY

Counseling
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Medical Genetics
Obstetrics and Gynecology
Pediatrics
Psychology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Patients
Physician Assistants
Physicians
Social Workers

GUIDELINE OBJECTIVE(S)

To assist health care professionals who provide genetic counseling and screening to consanguineous couples and their offspring

TARGET POPULATION

Consanguineous couples and their offspring in the United States and Canada

INTERVENTIONS AND PRACTICES CONSIDERED

1. Assessment, including family medical history and psychosocial history of the consultand(s)
2. Risk assessment through analysis of the pedigree and calculation of the inbreeding coefficient
3. Genetic testing and screening

   Fetus

   - Maternal-fetal serum marker for conditions such as neural tube defect
   - High-resolution fetal ultrasound

   Offspring

   - Standard neonatal screening
   - Filter paper blood spots by tandem mass spectrometry (MS/MS)
   - Hearing screening
   - Periodic well child checkups with primary care provider
4. Address psychosocial and multicultural issues

5. Follow-up
6. Provide education and support services through referral
7. Consider ethical and other special issues, such as adoption and incest

MAJOR OUTCOMES CONSIDERED

- Pregnancy outcome
- Morbidity and mortality in the first years of life for children from consanguineous unions

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developers searched the MEDLINE and PubMed databases (using the key words consanguinity and incest) to locate relevant English language medical papers published between 1965 and August 2000. Additional papers were identified through bibliographies of articles. Papers were reviewed with attention to genetic counseling and multicultural issues.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The literature was reviewed and evaluated according to the following categories outlined by the U.S. Preventive Services Task Force (1995).

I. Evidence obtained from at least one properly designed randomized controlled trial.

II-1. Evidence obtained from well-designed controlled trials without randomization.

II-2. Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3. Evidence obtained from multiple time series, with or without the intervention.

III. The opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The authoring committee sought expert review from specialists in North America. Opinions were sought from representatives of a support group for consanguineous couples (www.cousincouples.com). The recommendations were presented at the 2000 Annual Education Conferences of both the NSGC and the American Society of Human Genetics. They also were presented in September 2000 at the First International Workshop on Consanguinity, Endogamy and Cultural Diversity in Leeds, United Kingdom. A draft of the document was made available on the Internet to all members of the NSGC for comment (91% of the 1867 NSGC members are registered on the NSGC listserv). The NSGC membership includes genetic counselors, physicians, nurses, attorneys, PhD genetics professionals, social workers, and students. The NSGC Ethics Subcommittee (composed of seven

genetic counselors, and an ad hoc bioethicist/clergy representative) and an attorney for the NSGC reviewed the revised document. No conflicts with the NSGC Code of Ethics were identified in the final document. The NSGC Board of Directors unanimously approved the final document in May 2001.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The consensus of the guideline authors and reviewers is that beyond a thorough medical family history with follow-up of significant findings, no additional preconception screening is recommended for consanguineous couples. Consanguineous couples should be offered similar genetic screening as suggested for any couple of their ethnic group. During pregnancy, consanguineous couples should be offered maternal-fetal serum marker screening and high-resolution fetal ultrasonography. Newborns should be screened for impaired hearing and detection of treatable inborn errors of metabolism.

Primary Genetic Counseling Issues in Consanguinity

Assessment

Ascertain the client´s primary questions and concerns and mutually develop a plan to address these concerns.

Medical Family History

The consanguineous relationship should be documented in the form of a pedigree (see Figure 1 in the original guideline document). Patients often confuse degrees of relationships (e.g., confuse first cousins once removed with second cousins, or confuse step-relatives as being biologically related).

- Using standardized pedigree symbols obtain a comprehensive three or more generation pedigree from the consultand or proband. Include offspring, siblings, parents, grandparents, aunts, uncles, nieces, nephews, and first cousins of the consultand or proband, as appropriate.
- Consanguinity is noted on the pedigree with two parallel mating lines between the couple.

  Note in particular if any relatives have a medical history compatible with inborn errors of metabolism or other potentially genetic disorders.

- Verify potential genetic disorders with medical records, if possible. Consider referral for clinical genetic evaluation of individual(s) suspected to be affected with a genetic condition, as needed.
- Provide a genetic risk assessment for carrier status and the chances of affected offspring if autosomal recessive disorders or other inherited conditions are identified.
- Offer genetic testing depending on test availability, as appropriate.

Note the ethnicity of all grandparents and offer genetic screening appropriate for any couple of that ethnic background (e.g., cystic fibrosis testing for a Caucasian couple, hemoglobinopathy and thalassemia screening for African American couples or those of Caribbean descent, thalassemia screening for couples of Eastern Mediterranean or Asian background, etc.).

Maintain confidentiality of the family history with respect to the consultand(s) and extended family members.

Psychosocial History of the Consultand(s)

Attempt to build a relationship with the consultand(s) by validating feelings, empathizing, and listening. For each consultand, assess and address:

- Level of comprehension and communication
- Level of education, employment, and social functioning
- Perceived risk and perceived burden of risk; clarify any family myths and misconceptions about risks
- Coping skills
- Family/community support structure; discuss any stigma that the consultand(s) may perceive from family and peers
- Cultural beliefs about causation of birth defects and risks to offspring associated with consanguinity

Risk Assessment

Analyze the pedigree. Calculate the coefficient of inbreeding if multiple loops of consanguinity are present.

Offer genetic testing and screening as appropriate (see "Genetic Screening and Testing for Consanguineous Couples and Their Offspring" in the original guideline document).

Psychosocial Issues

In the United States there is significant stigma associated with consanguineous relationships. Mistaken societal beliefs in the "ills of cousin unions" are deeply ingrained as noted by Dr Bell, a New England physician in 1859:

> Perhaps no opinion, upon subjects of a medical character, is more widely diffused among the public, or more tenaciously held, than that the results of the marriage of blood relations are almost uniformly unfortunate. This opinion has been so long held and so often reiterated, that by sheer force of these circumstances alone it has come to be regarded as an unquestioned and unquestionable fact.

The history of hemophilia in the royal families of Europe in the 18th and 19th centuries is often cited as an example of the detrimental effects of inbreeding, even though the inheritance of this X-linked recessive condition would have occurred regardless of the consanguineous unions in the Royal families.

A key component of genetic counseling is to ascertain the client´s preconceived notion of the nature and magnitude of genetic risks to their offspring. If the client is from a culture where consanguineous unions are uncommon, discussing how frequent consanguineous unions occur in other parts of the world can be reassuring. Providing historical examples of cousin couples may also help to "normalize" their situation (e.g., Charles Darwin and his wife Emma Wedgwood were first cousins, as were Albert Einstein and his second wife Elsa Einstein; Queen Elizabeth II and her husband Prince Philip are related as closer than third cousins, etc.).

Consanguineous couples may keep their relationship hidden because of fears of stigma, discrimination, ostracization, and even legal prosecution. Discussing such fears and the attitudes of family and friends regarding their relationship is important. If a consanguineous couple has a child with a congenital anomaly or a genetic disorder, there may be an attitude of "I told you so" among family members and acquaintances, adding to feelings of parental guilt. Providing a follow-up letter after the genetic counseling session can clarify misconceptions that may circulate among the couple´s family and peers.

Shame reactions to perceived or actual external disapproval, ridicule, and scorn are also prominent in these families, particularly in the United States where consanguinity has been traditionally frowned upon. Excellent reviews have been written on the management of guilt and shame reactions in a genetic counseling setting.

Psychosocial counseling concerning incestuous unions is complex, particularly if the union involves a minor. Referral to specialized therapists and community support services is indicated if such services are not already in place.

Identification of positive carrier status may alter the person´s self-concept. There may be an altered perception of genetic identity, changed relationships with the family of origin, damage to self-esteem, altered social identity, altered perception of health, and a threat to the parental role.

Multicultural Issues

Immigrants to the United States and Canada from populations where consanguineous unions are common may have attitudes about the preference of consanguineous unions that are deeply embedded in cultural beliefs. Factors include the desirability of familiarity with the family´s social and biological traits, and possible better treatment by in-laws. There may be an economic rationale for keeping goods and property within a family. Genetic counseling should explore the client´s cultural belief systems while being respectful of client beliefs and cultural traditions.

Follow-up

Arrange/facilitate additional appointments to complete the family history, risk assessment, and testing considerations as indicated. Assist in referrals for evaluation of abnormal tests or screening results (e.g., abnormal ultrasound, positive neonatal screening, etc.).

A letter to the consultand(s) that includes a summary of major topics discussed in the genetic counseling session is helpful. The consultand(s) may also choose to share the letter to educate family members and health professionals.

Provide the consultand/couple with names of support groups and resources (see "Patient Resources" field of this NGC summary).

Ethical Issues and Special Considerations

See the original guideline document for information about (1) genetic testing for the child of a consanguineous union placed for adoption, (2) confirming parentage when incest is suspected, (3) populations with high mean coefficients of inbreeding, (4) pedigrees with multiple loops of consanguinity, and (5) legal ramifications of consanguineous unions.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

All supporting evidence is class III, opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees. No supporting literature of categories I or II was identified. See "Methods Used to Assess the Quality and Strength of the Evidence" field of this NGC summary.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Provide risk assessment and reproductive options to consanguineous couples who request genetic counseling in a preconception setting
- Improve pregnancy outcome and provide reproductive options when parental consanguinity is identified in a pregnancy
- Reduce morbidity and mortality in the first years of life for children from consanguineous unions
- Consider psychosocial and multicultural issues related to genetic counseling for consanguineous couples, with a focus on nonincestuous relationships

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The genetic counseling recommendations of the National Society of Genetic Counselors (NSGC) are developed to assist practitioners and patients in making decisions about appropriate management of genetic concerns. Each practice recommendation focuses on a clinical or practice issue and is based on a review and analysis of the professional literature. The information and recommendations reflect scientific and clinical knowledge current as of the publication date and are subject to change as advances in diagnostic techniques, treatments, and psychosocial understanding emerge. In addition, variations in practice, taking into account the needs of the individual patient and the resources and limitations unique to the institution or type of practice, may warrant alternative approaches, treatments, or procedures to the recommendations outlined in this document. Therefore, these recommendations should not be construed as dictating an exclusive course of management, nor does use of such recommendations guarantee a particular outcome. Genetic counseling recommendations do not displace a health care provider´s best medical judgment.
- These recommendations do not address the legal ramifications of consanguineous unions, which are unique to each state in the United States. Although the medical and genetic consequences of biological incest are reviewed in these recommendations, the psychosocial considerations are very different from those of cousin unions. There is a major attitudinal difference regarding a union involving consenting adult cousins as compared to incestuous abuse of a minor. Unions between cousins are the primary focus of the guideline.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Bennett RL, Motulsky AG, Bittles A, Hudgins L, Uhrich S, Doyle DL, Silvey K, Scott CR, Cheng E, McGillivray B, Steiner RD, Olsen D. Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the National Society of Genetic Counselors. J Genet Counsel 2002 Apr;11(2):97-119. [74 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Apr

GUIDELINE DEVELOPER(S)

National Society of Genetic Counselors

SOURCE(S) OF FUNDING

This project was supported by a special projects grant from the National Society of Genetic Counselors and by Grant #5H46 MC00091-16 from the Maternal and Child Health Bureau (Title V Social Security Act), Health Resources and Services Administration, Department of Health and Human Services, to the Pacific Northwest Regional Genetic Group (PacNoRGG).

GUIDELINE COMMITTEE

Consanguinity Working Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

The authoring subcommittee (Consanguinity Working Group [CWG]) consisted of experts in genetic counseling, medical genetics, public health genetics, genetic epidemiology, biochemical genetics, pediatric genetics, and perinatology. The Consanguinity Working Group included non-National Society of Genetic Counselors (NSGC) members. Input was also sought from an advocacy group for cousins who are romantically involved.

Working Group Members: Robin L. Bennett, Arno G. Motulsky, Alan Bittles, Louanne Hudgins, Stefanie Uhrich, Debra Lochner Doyle, Kerry Silvey, C. Ronald Scott, Edith Cheng, Barbara McGillivray, Robert D. Steiner, Debra Olson

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available from the National Society of Genetic Counselors, 233 Canterbury Drive, Wallingford, PA 19086-7608; Web site: www.nsgc.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Bennett RL, Steinhaus KA, Uhrich SB, et al. Recommendations for standardized human pedigree nomenclature. Am J Hum Genet 1995;56:745-52 and J Genet Couns 1995;4:267-79.

Electronic copies: Not available at this time.

Reprints available from Robin L. Bennett, Medical Genetics, Box 357720, University of Washington Medical Center, Seattle, WA 98195-7720.

PATIENT RESOURCES

The Cousin Couples website (www.cousincouples.com) provides access to support services for cousins who are romantically involved.

NGC STATUS

This NGC summary was completed by ECRI on January 9, 2003. The information was verified by the guideline developer on March 11, 2003.

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